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(54) Title: COMPOSITIONS AND METHODS FOR DELIVERY OF GENETIC MATERIAL

(57) Abstract

Methods of introducing genetic material into cells of an individual and compositions and kits for practicing the same are disclosed. The methods comprise the steps of contacting cells of an individual with a genetic vaccine facilitator and administering to the cells a nucleic acid molecule that is free of retroviral particles. The nucleic acid molecule comprises a nucleotide sequence that encodes a protein that comprises at least one epitope that is identical or substantially similar to an epitope of a pathogen antigen or an antigen associated with a hyperproliferative or autoimmune disease, a protein otherwise missing from the individual due to a missing, non-functional or partially functioning gene, or a protein that produces a therapeutic effect on an individual. Methods of prophylactically and therapeutically immunizing an individual against HIV are disclosed. Pharmaceutical compositions and kits for practicing methods of the present invention are disclosed.

Claims

1. A method of introducing genetic material into cells of an individual comprising the steps of:

a) contacting cells of said individual with a genetic vaccine facilitator selected from the group consisting of: anionic lipids; saponins; lectins; estrogenic compounds; hydroxylated lower alkyls; dimethyl sulfoxide; and urea; and,

b) administering to cells of said individual, a nucleic acid molecule;

wherein said nucleic acid molecule is free of retroviral particles.

2. The method of claim 1 wherein said genetic vaccine facilitator is an anionic lipid selected from the group consisting of: salts of lauric and oleic acids, lauric and oleic acids, acid esters of lauryl and cetyl alcohol, and sulfonates.

3. The method of claim 1 wherein said genetic vaccine facilitator is an anionic lipid selected from the group consisting of: sodium lauryl sulfate and oleic acid.

4. The method of claim 1 wherein said genetic vaccine facilitator is a saponin selected from the group consisting of: saponarin, sarmentocymarin and sapogenins.

5. The method of claim 1 wherein said genetic vaccine facilitator is a saponin selected from the group consisting of: sarmentogenin, sarsasapogenin and sarverogenin.

6. The method of claim 1 wherein said genetic vaccine facilitator is a lectin selected from the group consisting of: concanavalin A, abrin, soybean agglutinin and wheat germ agglutinin.

7. The method of claim 1 wherein said genetic vaccine facilitator is a lectin selected from the group consisting of: concanavalin A.

8. The method of claim 1 wherein said genetic vaccine facilitator is β-estradiol.

9. The method of claim 1 wherein said genetic vaccine facilitator is selected from the group consisting of: ethanol, n-propanol, isopropanol and n-butanol.

10. The method of claim 1 wherein said genetic vaccine facilitator is dimethyl sulfoxide.

11. The method of claim 1 wherein said genetic vaccine facilitator is urea.

12. The method of claim 1 wherein said nucleic acid molecule comprises a nucleotide sequence that encodes a protein and is operably linked to regulatory sequences.

13. The method of claim 1 wherein said nucleic acid molecule comprises a nucleotide sequence that encodes a protein which comprises at least one epitope that is identical or substantially similar to an epitope of an antigen against which an immune response is desired, said nucleotide sequence operably linked to regulatory sequences.

14. A method of immunizing an individual against a pathogen comprising the steps of:

a) contacting cells of said individual with a genetic vaccine facilitator selected from the group consisting of: anionic lipids; saponins; lectins; estrogenic compounds; hydroxylated lower alkyls; dimethyl sulfoxide; and urea; and,

b) administering to cells of said individual, a nucleic acid molecule that comprises a nucleotide sequence that encodes a protein which comprises at least one epitope that is

identical or substantially similar to an epitope of a pathogen antigen, said nucleotide sequence being operably linked to regulatory sequences;

wherein said nucleic acid molecule is free of retroviral particles and said nucleotide sequence is capable of being expressed in said cells.

15. The method of Claim 14 wherein said genetic vaccine facilitator is selected from the group consisting of: sodium lauryl sulfate; oleic acid; saponarin; sarmentocymarin; sapogenins; sarmentogenin; sarsasapogenin; sarverogenin; concanavalin A; β-estradiol; ethanol; dimethyl sulfoxide; and urea.

16. The method of Claim 14 wherein said nucleic acid molecule is a DNA molecule.

17. The method of Claim 14 wherein said protein is a pathogen antigen or a fragment thereof.

18. The method of Claim 14 wherein said nucleic acid molecule is administered intramuscularly.

19. The method of Claim 14 wherein said pathogen is a virus selected from the group consisting of: human immunodeficiency virus, HIV; human T cell leukemia virus, HTLV; influenza virus; hepatitis A virus, HAV; hepatitis B virus, HBV; hepatitis C virus, HCV; human papilloma virus, HPV; Herpes simplex 1 virus, HSV1; Herpes simplex 2 virus, HSV2; Cytomegalovirus, CMV; Epstein-Barr virus, EBV; rhinovirus; and, coronavirus.

20. The method of Claim 14 wherein at least two or more different nucleic acid molecules are administered to different cells of an individual; said different nucleic acid molecules each comprise nucleotide sequences encoding one or more pathogen antigens of the same pathogen.

21. The method of Claim 14 wherein said genetic vaccine facilitator and said nucleic acid molecule are administered simultaneously.

22. A method of immunizing an individual against a disease comprising the steps of:

a) contacting cells of said individual with a genetic vaccine facilitator selected from the group consisting of: anionic lipids; saponins; lectins; estrogenic compounds; hydroxylated lower alkyls; dimethyl sulfoxide; and urea; and,

b) administering to cells of said individual, a nucleic acid molecule comprising a nucleotide sequence that encodes a target protein which comprises an epitope identical or substantially similar to an epitope of a protein associated with cells that characterize said disease operatively linked to regulatory sequences;

wherein said nucleic acid molecule is free of retroviral particles and capable of being expressed in said cells.

23. The method of Claim 22 wherein said genetic vaccine facilitator is selected from the group consisting of: sodium lauryl sulfate; oleic acid; saponarin; sarmentocymarin; sapogenins; sarmentogenin; sarsasapogenin; sarverogenin; concanavalin A; β-estradiol; ethanol; dimethyl sulfoxide; and urea.

24. The method of Claim 22 wherein said disease is characterized by hyperproliferating cells.

25. The method of Claim 22 wherein said disease is an autoimmune disease.

26. The method of Claim 22 wherein said nucleic acid molecule is a DNA molecule.

27. The method of Claim 22 wherein said nucleic acid molecule is administered intramuscularly.

28. The method of Claim 22 wherein said nucleic acid molecule comprises a nucleotide sequence that encodes a target protein selected from the group consisting of: protein products of oncogenes *myb, myc, fyn, ras, sarc, neu* and *trk*; protein products of translocation gene *bcl/abl;* P53; EGRF; variable regions of antibodies made by B cell lymphomas; and variable regions of T cell receptors of T cell lymphomas.

29. The method of Claim 22 wherein said protein is selected from the group consisting of: variable regions of antibodies involved in B cell mediated autoimmune disease; and variable regions of T cell receptors involved in T cell mediated autoimmune disease.

30. A method of treating an individual suspected of suffering from a disease comprising the steps of:

a) contacting cells of said individual with a genetic vaccine facilitator selected from the group consisting of anionic lipids; saponins; lectins; estrogenic compounds; hydroxylated lower alkyls; dimethyl sulfoxide; and urea; and,

b) administering to cells of said individual, a nucleic acid molecule comprising a nucleotide sequence that encodes a protein whose presence will compensate for a missing, non-functional or partially functioning protein or produce a therapeutic effect on the individual, said nucleotide sequence operatively linked to regulatory sequences;

wherein said nucleic acid molecule is free of retroviral particles and capable of being expressed in said cells.

31. The method of Claim 30 wherein said genetic vaccine facilitator is selected from the group consisting of: sodium lauryl sulfate; oleic acid; saponarin; sarmentocymarin; sapogenins; sarmentogenin; sarsasapogenin; sarverogenin;

concanavalin A; β-estradiol; ethanol; dimethyl sulfoxide; and urea.

32. The method of Claim 30 wherein said nucleic acid molecule is a DNA molecule.

33. The method of Claim 30 wherein said nucleic acid molecule is administered intramuscularly.

34. The method of Claim 30 wherein said nucleic acid molecule comprises a nucleotide sequence that encodes a protein selected from the group consisting of: enzymes, structural proteins, cytokines, lymphokines and growth factors.

35. A pharmaceutical composition comprising:

i) a nucleic acid molecule that comprises a nucleotide sequence which encodes a protein selected from the group consisting of: proteins which comprises at least one epitope that is identical or substantially similar to an epitope of a pathogen antigen; proteins which comprises an epitope identical or substantially similar to an epitope of a protein associated with hyperproliferating cells; proteins which comprises an epitope identical or substantially similar to an epitope of a protein associated with cells that characterize an autoimmune disease; proteins whose presence will compensate for a missing, non-functional or partially functioning protein in an individual; and proteins that produce a therapeutic effect on an individual; and

ii) a genetic vaccine facilitator selected from the group consisting of: anionic lipids; saponins; lectins; estrogenic compounds; hydroxylated lower alkyls; dimethyl sulfoxide; and urea;

wherein said pharmaceutical composition is free of retroviral particles.

36. The method of Claim 35 wherein said genetic vaccine facilitator is selected from the group consisting of: sodium

lauryl sulfate; oleic acid; saponarin; sarmentocymarin; sapogenins; sarmentogenin; sarsasapogenin; sarverogenin; concanavalin A; β-estradiol; ethanol; dimethyl sulfoxide; and urea.

37. A pharmaceutical kit comprising:

i) a container that comprises a nucleic acid molecule that comprises a nucleotide sequence which encodes a protein selected from the group consisting of: proteins which comprises at least one epitope that is identical or substantially similar to an epitope of a pathogen antigen; proteins which comprises an epitope identical or substantially similar to an epitope of a protein associated with hyperproliferating cells; proteins which comprises an epitope identical or substantially similar to an epitope of a protein associated with cells that characterize an autoimmune disease; proteins whose presence will compensate for a missing, non-functional or partially functioning protein in an individual; and proteins that produce a therapeutic effect on an individual; and

ii) a container that comprises a genetic vaccine facilitator selected from the group consisting of: anionic lipids; saponins; lectins; estrogenic compounds; hydroxylated lower alkyls; dimethyl sulfoxide; and urea;

wherein said pharmaceutical kit is free of retroviral particles.

38. The method of Claim 37 wherein said genetic vaccine facilitator is selected from the group consisting of: sodium lauryl sulfate; oleic acid; saponarin; sarmentocymarin; sapogenins; sarmentogenin; sarsasapogenin; sarverogenin; concanavalin A; β-estradiol; ethanol; dimethyl sulfoxide; and urea.

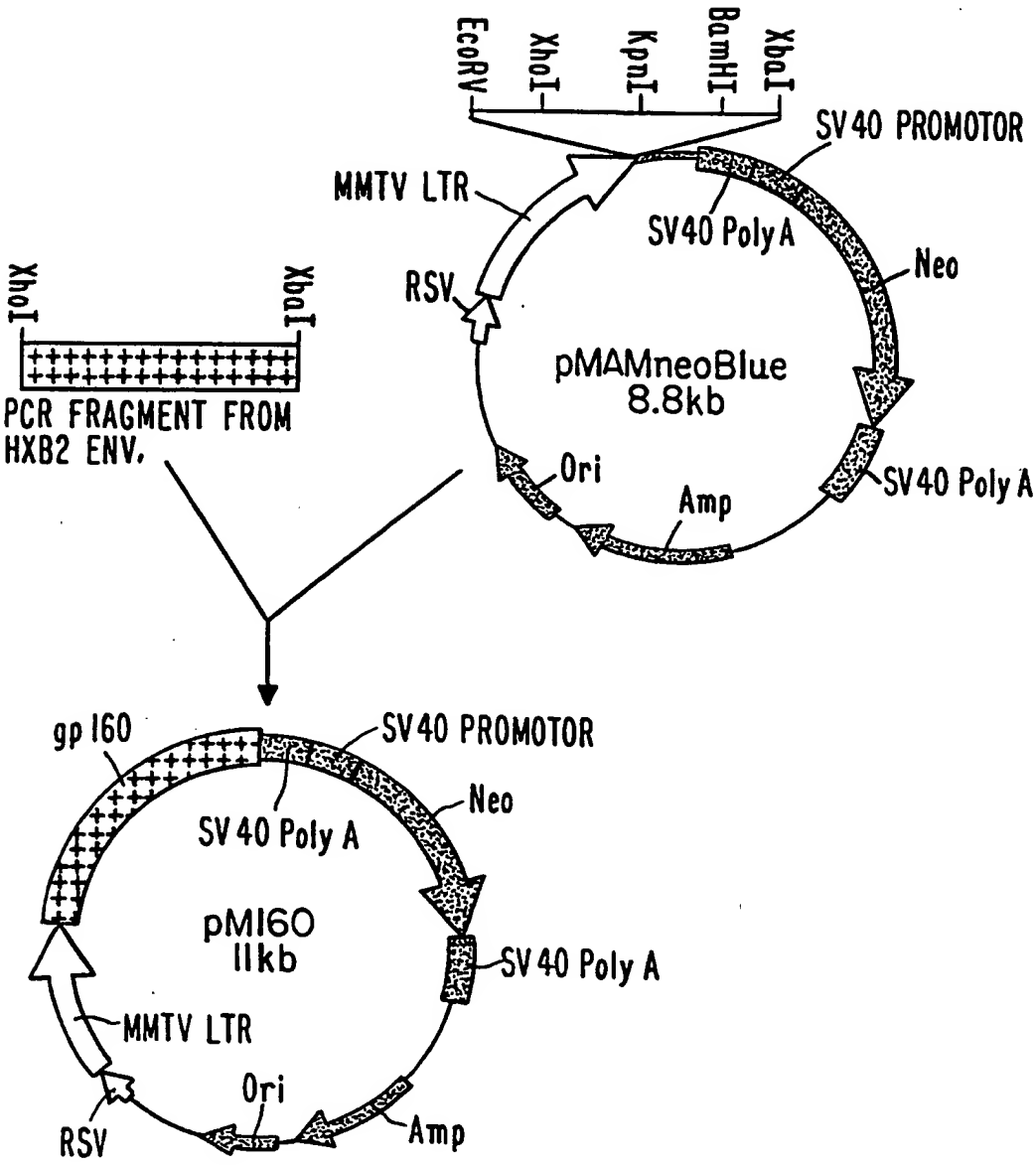
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Fig. 1

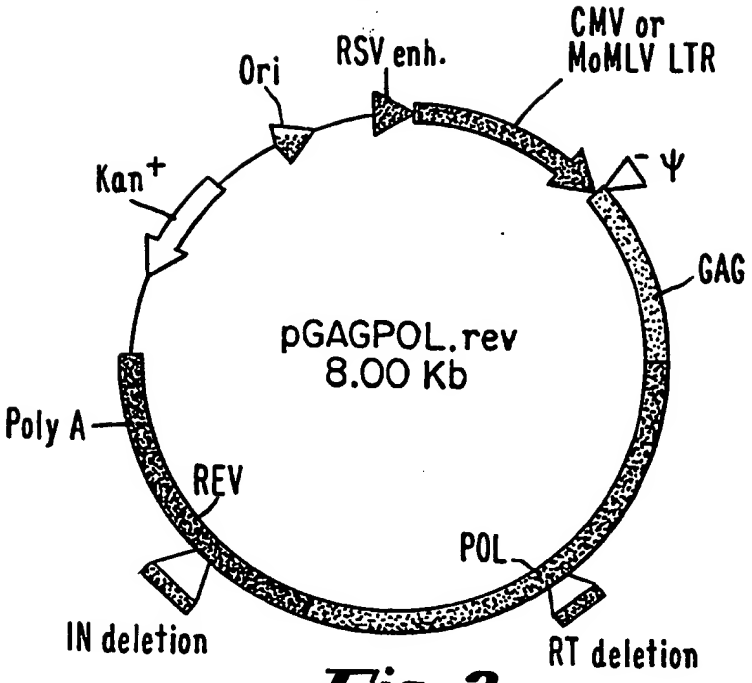

Fig. 2

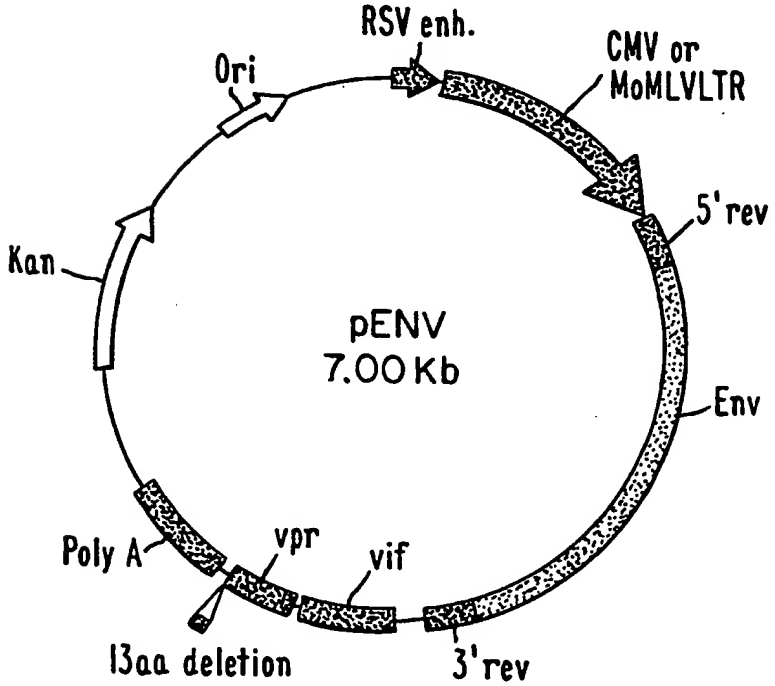

Fig. 3

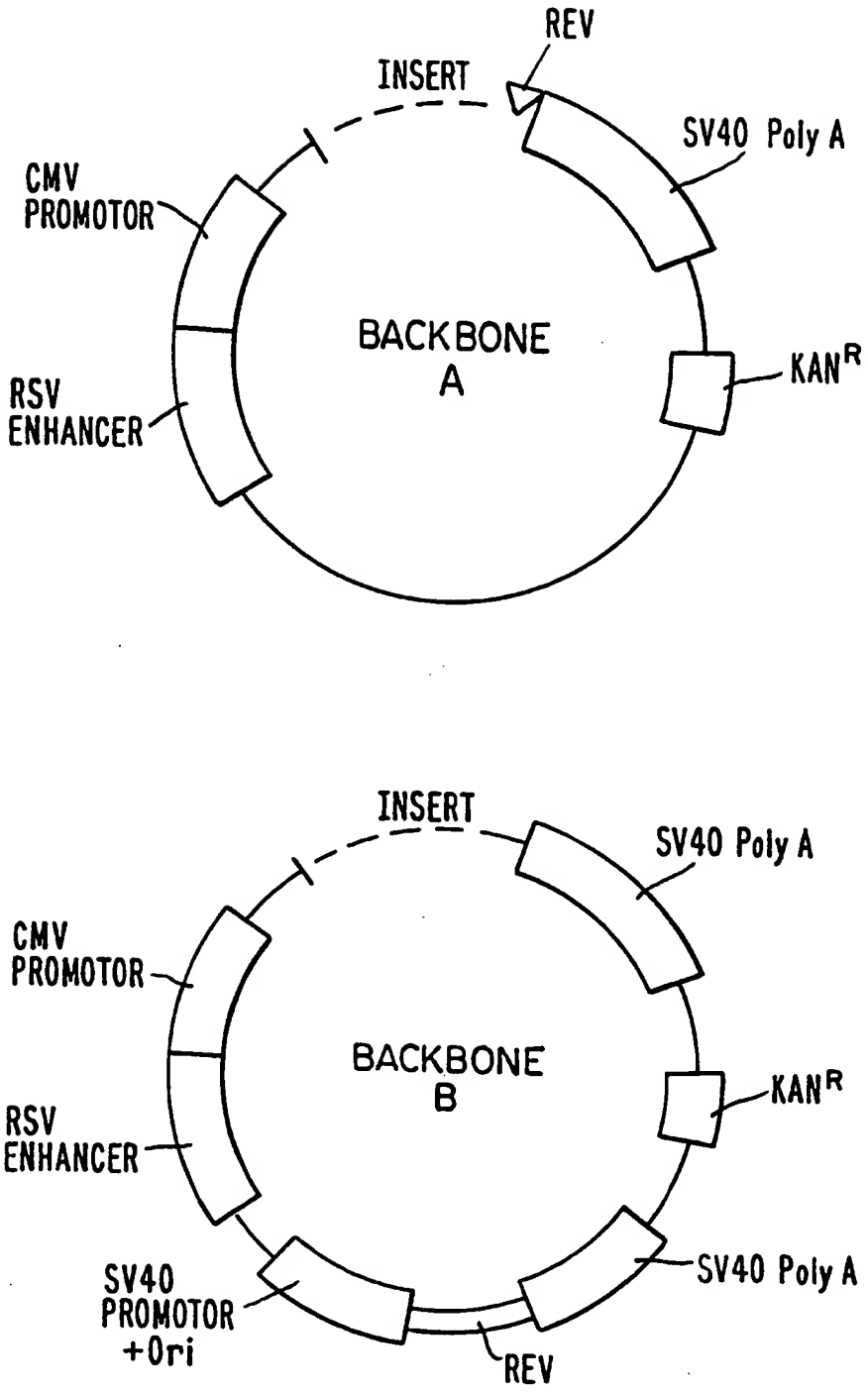
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Fig. 4a

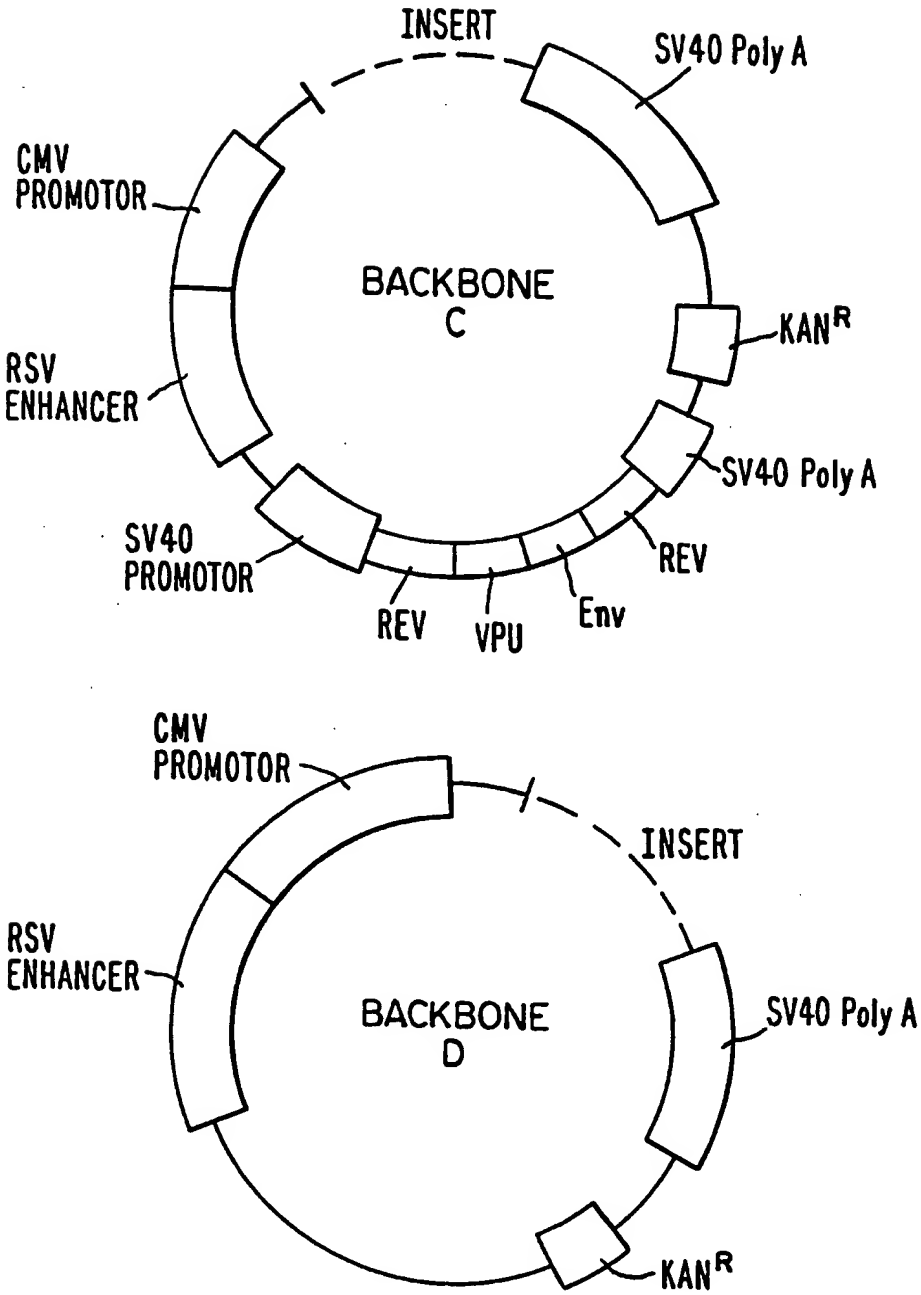
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Fig. 4b